

K is an L-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine, δ -N-2-imidazolinylnornithine, δ -N-benzylcarbamoylnornithine, and β -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

K' is a D-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine, δ -N-2-imidazolinylnornithine, δ -N-benzylcarbamoylnornithine, and β -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

L is independently selected at each occurrence from the group: glycine, L-alanine, and D-alanine;

M is L-aspartic acid;

M' is D-aspartic acid;


R¹ is an amino acid substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, phenylalanine, thienylalanine, phenylglycine, cyclohexylalanine, homophenylalanine, 1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, and methionine;

R² is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, L-phenylalanine, D-phenylalanine, thienylalanine, phenylglycine, biphenylglycine, cyclohexylalanine, homophenylalanine, L-1-naphthylalanine, D-1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, methionine, and 2-aminothiazole-4-acetic acid;

R³ is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine,

D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, and D-methionine;

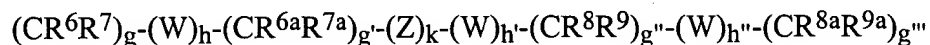
R⁴ is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, D-methionine, and 2-aminothiazole-4-acetic acid;

 R⁵ is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, L-valine, L-alanine, L-leucine, L-isoleucine, L-norleucine, L-2-aminobutyric acid, L-2-aminohexanoic acid, L-tyrosine, L-phenylalanine, L-thienylalanine, L-phenylglycine, L-cyclohexylalanine, L-homophenylalanine, L-1-naphthylalanine, L-lysine, L-serine, L-ornithine, L-1,2-diaminobutyric acid, L-1,2-diaminopropionic acid, L-cysteine, L-penicillamine, L-methionine, and 2-aminothiazole-4-acetic acid;

provided that one of R¹, R², R³, R⁴, and R⁵ in each Q is substituted with a bond to L_n, further provided that when R² is 2-aminothiazole-4-acetic acid, K is N-methylarginine, further provided that when R⁴ is 2-aminothiazole-4-acetic acid, K and K' are N-methylarginine, and still further provided that when R⁵ is 2-aminothiazole-4-acetic acid, K' is N-methylarginine;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

L_n is a linking group having the formula:




provided that $g+h+g'+k+h'+g''+h''+g'''$ is other than 0;

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁰;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹ and R^{9a} are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁₋₅ alkyl substituted with 0-3 R¹⁰, aryl substituted with 0-3 R¹⁰, benzyl substituted with 0-3 R¹⁰, and C₁₋₅ alkoxy substituted with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to C_h;

 R¹⁰ is independently selected at each occurrence from the group: a bond to C_h, COOR¹¹, OH, NHR¹¹, SO₃H, PO₃H, aryl substituted with 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy substituted with 0-1 R¹², and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹¹;

R¹¹ is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R¹², a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², C₃₋₁₀ cycloalkyl substituted with 0-1 R¹², polyalkylene glycol substituted with 0-1 R¹², carbohydrate substituted with 0-1 R¹², cyclodextrin substituted with 0-1 R¹², amino acid substituted with 0-1 R¹², polycarboxyalkyl substituted with 0-1 R¹², polyazaalkyl substituted with 0-1 R¹², peptide substituted with 0-1 R¹², wherein the peptide is comprised of 2-10 amino acids, and a bond to C_h;

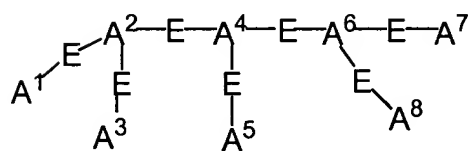
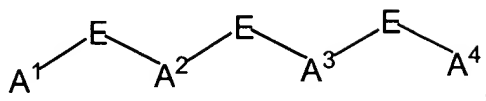
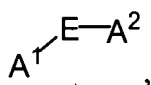
R¹² is a bond to C_h;

k is selected from 0, 1, and 2;

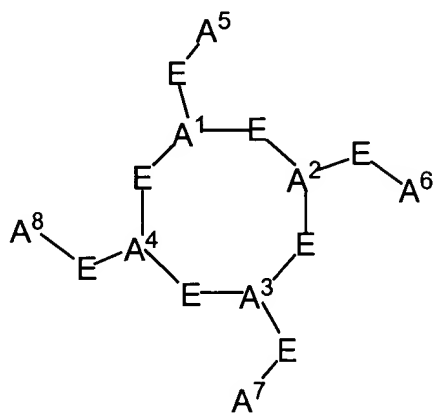
h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;
h'' is selected from 0, 1, 2, 3, 4, and 5;
g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g''' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

C_h is a metal bonding unit having a formula selected from the group:



, and




;

A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group N, NR¹³, NR¹³R¹⁴, S, SH, S(Pg), O, OH, PR¹³, PR¹³R¹⁴, P(O)R¹⁵R¹⁶, and a bond to L_n;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group:
C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆₋₁₀ aryl-C₁₋₁₀ alkyl substituted

with 0-3 R¹⁷, C₁₋₁₀ alkyl-C₆₋₁₀ aryl- substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹³, and R¹⁴ are each independently selected from the group: a bond to L_n, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₁₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆₋₁₀ aryl-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl-C₆₋₁₀ aryl- substituted with 0-3 R¹⁷, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷, and an electron, provided that when one of R¹³ or R¹⁴ is an electron, then the other is also an electron;

 alternatively, R¹³ and R¹⁴ combine to form =C(R²⁰)(R²¹);

R¹⁵ and R¹⁶ are each independently selected from the group: a bond to L_n, -OH, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆₋₁₀ aryl-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl-C₆₋₁₀ aryl- substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

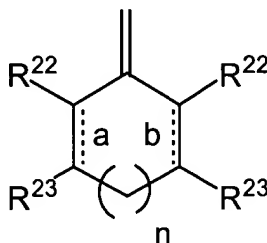
R¹⁷ is independently selected at each occurrence from the group: a bond to L_n, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R¹⁸, -C(=O)R¹⁸, -C(=O)N(R¹⁸)₂, -CHO, -CH₂OR¹⁸, -OC(=O)R¹⁸, -OC(=O)OR^{18a}, -OR¹⁸, -OC(=O)N(R¹⁸)₂, -NR¹⁹C(=O)R¹⁸, -NR¹⁹C(=O)OR^{18a}, -NR¹⁹C(=O)N(R¹⁸)₂, -NR¹⁹SO₂N(R¹⁸)₂, -NR¹⁹SO₂R^{18a}, -SO₃H, -SO₂R^{18a}, -SR¹⁸, -S(=O)R^{18a}, -SO₂N(R¹⁸)₂, -N(R¹⁸)₂, -NHC(=S)NHR¹⁸, =NOR¹⁸, NO₂, -C(=O)NHOR¹⁸, -C(=O)NHN(R¹⁸)R^{18a}, -OCH₂CO₂H, 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl, aryl substituted with 0-2 R¹⁸, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

R¹⁸, R^{18a}, and R¹⁹ are independently selected at each occurrence from the group: a bond to L_n, H, C₁-C₆ alkyl, phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and trifluoromethyl;

Pg is a thiol protecting group;

R²⁰ and R²¹ are independently selected from the group: H, C₁-C₁₀ alkyl, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂, C₂-C₁₀ 1-alkene substituted with 0-3 R²³, C₂-C₁₀ 1-alkyne substituted with 0-3 R²³, aryl substituted with 0-3 R²³, unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and unsaturated C₃₋₁₀ carbocycle substituted with 0-3 R²³;

alternatively, R²⁰ and R²¹, taken together with the divalent carbon radical to which they are attached form:



R²² and R²³ are independently selected from the group: H, R²⁴, C₁-C₁₀ alkyl substituted with 0-3 R²⁴, C₂-C₁₀ alkenyl substituted with 0-3 R²⁴, C₂-C₁₀ alkynyl substituted with 0-3 R²⁴, aryl substituted with 0-3 R²⁴, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²⁴, and C₃₋₁₀ carbocycle substituted with 0-3 R²⁴;

alternatively, R²², R²³ taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

a and b indicate the positions of optional double bonds and n is 0 or 1;

R²⁴ is independently selected at each occurrence from the group: =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂, -N(R²⁵)₃⁺, -CH₂OR²⁵, -OC(=O)R²⁵, -OC(=O)OR^{25a}, -OR²⁵, -OC(=O)N(R²⁵)₂, -NR²⁶C(=O)R²⁵, -NR²⁶C(=O)OR^{25a},

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anal
-NR²⁶C(=O)N(R²⁵)₂, -NR²⁶SO₂N(R²⁵)₂, -NR²⁶SO₂R^{25a}, -SO₃H, -SO₂R^{25a}, -SR²⁵,
-S(=O)R^{25a}, -SO₂N(R²⁵)₂, -N(R²⁵)₂, =NOR²⁵, -C(=O)NHOR²⁵, -OCH₂CO₂H, and
2-(1-morpholino)ethoxy; and,

R²⁵, R^{25a}, and R²⁶ are each independently selected at each occurrence from the group: hydrogen
and C₁-C₆ alkyl;

and a pharmaceutically acceptable salt thereof.

B2
12. (Amended) A composition according to Claim 11, wherein the
metallopharmaceutical is a diagnostic radiopharmaceutical, the metal is a radioisotope selected
from the group: ^{99m}Tc, ⁹⁵Tc, ¹¹¹In, ⁶²Cu, ⁶⁴Cu, ⁶⁷Ga, and ⁶⁸Ga, the targeting moiety is a
peptide or a mimetic thereof and the linking group is present between the targeting moiety and
chelator.

13. (Amended) A composition according to Claim 12, wherein the targeting moiety is a
cyclic pentapeptide.

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19. (Amended) A composition according to Claim 11, wherein the
metallopharmaceutical is a therapeutic radiopharmaceutical, the metal is a radioisotope selected
from the group: ¹⁸⁶Re, ¹⁸⁸Re, ¹⁵³Sm, ¹⁶⁶Ho, ¹⁷⁷Lu, ¹⁴⁹Pm, ⁹⁰Y, ²¹²Bi, ¹⁰³Pd, ¹⁰⁹Pd, ¹⁵⁹Gd,
¹⁴⁰La, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁶⁵Dy, ¹⁶⁶Dy, ⁶⁷Cu, ¹⁰⁵Rh, ¹¹¹Ag, and ¹⁹²Ir, the targeting
moiety is a peptide or a mimetic thereof and the linking group is present between the targeting
moiety and chelator.

20. (Amended) A composition according to Claim 19, wherein the targeting moiety is a
cyclic pentapeptide.

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27. (Amended) A composition according to Claim 11, wherein the
metallopharmaceutical is a MRI contrast agent, the metal is a paramagnetic metal ion selected
from the group: Gd(III), Dy(III), Fe(III), and Mn(II), the targeting moiety is a peptide or a
mimetic thereof and the linking group is present between the targeting moiety and chelator.

28. (Amended) A composition according to Claim 27, wherein the targeting moiety is a
cyclic pentapeptide.

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31. (Amended) A composition according to Claim 11, wherein the metallopharmaceutical is a X-ray contrast agent, the metal is selected from the group: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir, the targeting moiety is a cyclic pentapeptide, and the linking group is present between the targeting moiety and chelator.
